Phosphatidylserine directly and positively regulates fusion of myoblasts into myotubes.

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Public Summary:
This work finds novel ways to promote better formation of skeletal muscle from muscle progenitor cells, which could be used for enhancing muscle healing in people with acquired or genetic myopathies.

Scientific Abstract:
Cell membrane consists of various lipids such as phosphatidylserine (PS), phosphatidylcholine (PC), and phosphatidylethanolamine (PE). Among them, PS is a molecular marker of apoptosis, because it is located to the inner leaflet of plasma membrane generally but it is moved to the outer leaflet during programmed cell death. The process of apoptosis has been implicated in the fusion of muscle progenitor cells, myoblasts, into myotubes. However, it remained unclear whether PS regulates muscle cell differentiation directly. In this paper, localization of PS to the outer leaflet of plasma membrane in proliferating primary myoblasts and during fusion of these myoblasts into myotubes is validated using Annexin V. Moreover, we show the presence of PS clusters at the cell-cell contact points, suggesting the importance of membrane ruffling and PS exposure for the myogenic cell fusion. Confirming this conclusion, experimentally constructed PS, but not PC liposomes dramatically enhance the formation of myotubes from myoblasts, thus demonstrating a direct positive effect of PS on the muscle cell fusion. In contrast, myoblasts exposed to PC liposomes produce long myotubes with low numbers of myonuclei. Moreover, pharmacological masking of PS on the myoblast surface inhibits fusion of these cells into myotubes in a dose-dependent manner.